Alkane Hydroxylation by a Manganese Analogue of the Iron Core from Methane Monooxygenase

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A binuclear manganese (II/II) complex with a μ-hydroxo bridging ligand catalyses the hydroxylation of cyclohexane in the presence of *tert*-butyl hydroperoxide (TBHP).

Biomimetic models of methane monooxygenase enzyme (MMO) have been extensively studied in association with alkane functionalization reactions.[1] Spectroscopic studies on the MMO enzyme clearly demonstrated that the catalytic site is occupied by a μ-hydroxo diiron core [Fe_2(μ-OH)], together with carboxylate anions (terminal and bridging) and a terminal aqua ligand.[2] A few iron complexes have been proposed as structural models of the MMO enzyme,[3] but no manganese analogue of the active site has been reported, although manganese complexes [particularly those containing the di-μ-oxo dimanganese(III/IV) core] are known to exhibit MMO activity.[4] Here we report the synthesis and alkane functionalization properties of a manganese complex which possesses a μ-hydroxo dimanganese(II/II) core.

The synthesis of the macrocyclic ligand with 2-pyridylmethyl pendant arms (L) was conducted according to classical procedure. The macrocyclic free base 1,4,10,13-tetraaza-7,16-dioxacyclooctadecane[5]† was prepared by condensation of the disodium salt of *N,N*′-ditosylethylenediamine with 6,9-ditosyl-6,9-diaza-1,14-tosyloxy-3,12-dioxatetradecane according to the procedure of Richman and Atkins.[6] Deprotection of the *N*-tosyl groups with HBr–acetic acid afforded the tetrahydrobromide salt in 82% yield. The four 2-picolyl groups were introduced by alkylation of the free base with 2-chloromethyl pyridine in MeCN in the presence of potassium carbonate.‡ The manganese complex $Mn_2L(OH)(ClO_4)_3$ **1** was prepared by mixing hydrated metal acetate and the ligand L (1 : 1) in MeOH and the addition of a small excess of sodium perchlorate afforded a white solid (75% yield). We failed to isolate a μ-acetato bridged complex, but X-ray crystallography revealed that a hydroxo ligand was present between the two metal centres.

Crystals of **1** suitable for single crystal X-ray diffraction studies were obtained by slow crystallization from an aqueous solution.§ A representation of the structure, in which the hydrogen atoms and the counter anions have been omitted, is proposed in Fig. 1.

In the solid state, the two manganese(II) atoms are surrounded by four nitrogens (two from the pyridine ligands and two from the macrocycle) and two oxygen atoms, one from a bridging hydroxo ligand, the other from an ether function. The complex is highly symmetrical with respect to the two metal centres. The presence of a twofold axis (C_2) perpendicular to the mid-plane of the macrocycle confirms that the two metal centres are at the same +2 oxidation level [the EPR spectrum is not consistent with a fully delocalized mixed valence (2/3) complex]. To ensure the neutrality of the complex, the bridging ligand must be a hydroxo ligand. A hydrogen bond effectively exists between the hydroxy group and one oxygen atom of a disordered perchlorate anion. The geometry around the metal centres is highly distorted. Four atoms [N(1), N(12), O and O(1)] are nearly coplanar, the two other axial bonds are inclined towards the nitrogen part of the ligand. An interesting feature of this complex is the fact that for each manganese there is a labile coordination position occupied by O(1) and O(2) from ether functions. These coordinating atoms could be easily replaced by a peroxide and could play a role similar to the labile water molecule that is present in the diferrous core of the MMO enzyme.

Our attempts to oxidize this manganese(II) dimer with H_2O_2 in slightly alkaline aqueous solution were unsuccessful. The solution turned light green and the colour rapidly disappeared with concomitant deposit of manganese dioxide. We were able to isolate light green crystals by reacting the macrocyclic ligand L with manganese(III) acetate in MeCN solution for four days, but the determination of the stoichiometry of the complex is not yet completed.

We performed a hydroxylation reaction of cyclohexane with our complex. In a typical reaction, cyclohexane (3.75 mmol) was treated with TBHP (660 μmol) in MeCN (5 ml) in the presence of the manganese catalyst (3.75 μmol; cyclohexane : TBHP : catalyst 1000 : 175 : 1) at 25 °C in an air atmo-

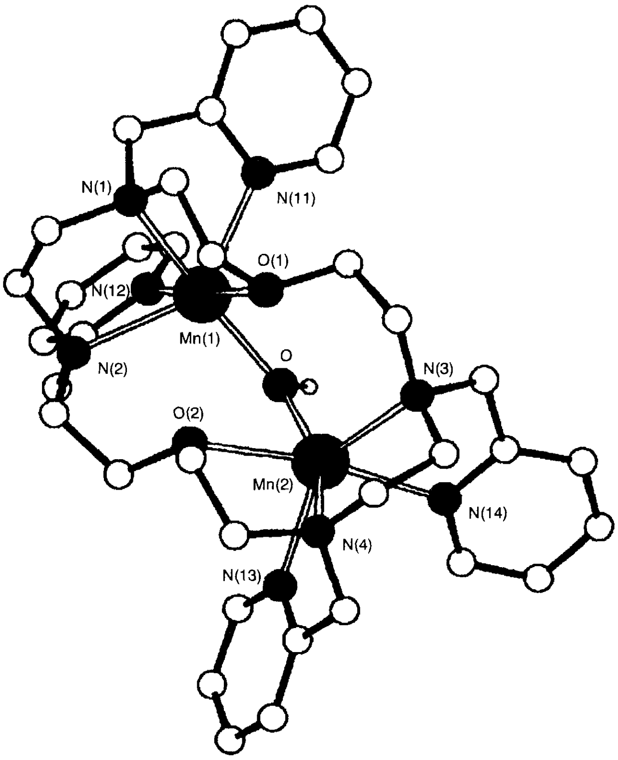

Fig. 1 Structure of the cation $[Mn_2(OH)L]^{3+}$ showing the atom labelling scheme. Selected interatomic distances (Å) and angles (°) Mn(1)–O 2.021(3), Mn(2)–N(3) 2.342(3), N(12)–Mn(1)–N(2) 73.11(10), Mn(1)–N(11) 2.261(3), Mn(2)–O(2) 2.338(2), N(1)–Mn(1)–N(2) 77.88(10), Mn(1)–N(12) 2.301(3), Mn(1)–Mn(2) 3.615(4), N(12)–Mn(1)–O(1) 171.67(9), Mn(1)–N(1) 2.333(3), Mn(1)–O–Mn(2) 126.77(11), O–Mn(2)–N(14) 112.88(10), Mn(1)–N(2) 2.340(3), O–Mn(1)–N(11) 110.55(10), N(13)–Mn(2)–N(14) 85.02(10), Mn(2)–O 2.026(2), O–Mn(1)–N(12) 103.25(9), O–Mn(2)–O(2) 82.35(9), Mn(2)–N(13) 2.288(3), N(11)–Mn(1)–N(12) 85.99(10), O–Mn(1)–O(1) 82.89(8), Mn(2)–N(14) 2.304(3), O–Mn(1)–N(2) 106.50(10), N(4)–Mn(2)–N(3) 77.46(10), Mn(2)–N(4) 2.334(3), N(11)–Mn(1)–N(1) 73.55(10), N(13)–Mn(2)–O(2) 174.69(9).

sphere. The reaction was monitored by GC analysis, and the amounts of both cyclohexanol and cyclohexanone were estimated with the aid of an internal standard (anisole). The yield of the different oxidation products was the same when the reaction was performed with the manganese(II) dimer or a 1 : 2 mixture of the ligand and $MnCl_2 \cdot 4H_2O$ (20 and 18 turnovers for cyclohexanone and cyclohexane, respectively; total chemical yield 34%). The reaction proceeds more rapidly when it is performed with a mixture of the ligand and manganese chloride as it is completed in 6 *vs.* 24 h for the manganese(II) dimer. Interestingly, catalyst **1** was not altered during the catalytic cycle, as a second addition of TBHP after 24 h doubled the amount of cyclohexanol and cyclohexanone. Thus, the activity of the catalyst appeared not to be modified by oxidative conditions.

Further experiments will be conducted in order to determine the nature of the active oxidizing species and particularly its oxidation level. Mixed valence (III/IV) oxidation states have been frequently involved in oxidation reactions performed with manganese dimers. In the present case, this oxidation state seems to be difficult to obtain in aqueous solution. We are currently attempting to prepare ligands possessing more electron donor chelating groups than pyridine heterocycles in order to stabilize higher oxidation levels of manganese.

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Footnotes

† This compound has been previously prepared by another procedure.

‡ Yield 31%, mp 95–96 °C (MeCN). ^{1}H NMR ($CDCl_3$) δ 2.73 (t, 8H), 2.86 (s, 8H), 3.57 (t, 8H), 3.78 (s, 8H), 7.1–7.57 (m, 12H), 8.48 (d, 4H). MS *m/z* 624 (M^+), 532 (M − 92).

§ *Crystal data* for **1**: $C_{36}H_{48}N_8O_2Mn_2(OH)(ClO_4)_3$, H_2O, monoclinic $P2_1/n$, a = 29.433 (14), b = 17.694 (9), c = 9.007 (5) Å, β = 104.66 (5)°, V = 4538(4) Å^3, $Z = 4$, F_w = 1062.7, D_x = 1.51 g cm^{-3}, Mo-Kα radiation (λ = 0.71073 Å), μ = 0.85 mm^{-1}, 294 K, $F(000)$ = 2208. A crystal of about 0.65 × 0.6 × 0.6 mm was mounted on a Philips PW1100 diffractometer using graphite monochromated Mo-Kα radiation. The data collection was performed under the following conditions: ω/2θ mode, speed 0.03° s^{-1}, width 1.0°, max. 2θ 56°. The structure was solved with SHELXS86 and refined with SHELX93 programs, using anisotropic thermal parameters. Most of hydrogen atoms, and particularly the hydrogen bonded to the bridging oxygen, were located on Fourier-difference syntheses, and all were introduced at calculated positions (C–H = 1 Å). One of the free perchlorate anions is disordered (occupation factors 0.8/0.2) and a water molecule was located hydrogen-bonded to the oxygens of two different perchlorates anions [O(32)–O(W)–O(33) = 121°, O(32)–O(W) = 3.2 Å, O(W)–O(33) = 2.9 Å, water hydrogens not located]. Another hydrogen bond exists between the hydroxy group and one oxygen atom of the disordered perchlorate anion [O–O(23) = 2.91 Å, O–H = 0.7 Å, O–H–O(23) = 174°]. The final conventional R factor is 0.039 for 5700 reflections with $I > 2\sigma(I)$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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